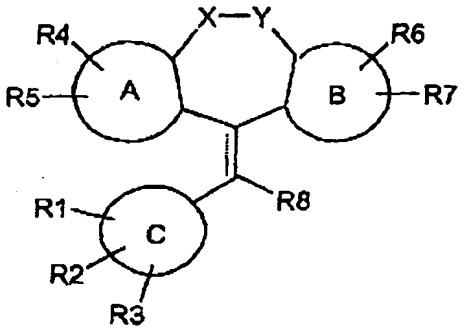
R^8 represents hydrogen, halo, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl , (C_1-C_4)alkyl - (C_1-C_6)alkoxy, COR^{12} wherein R^{12} represents methoxy, ethoxy, hydroxymethyl, or methoxymethyl; (C_3-C_7)cycloalkyl, aryl or substituted aryl.

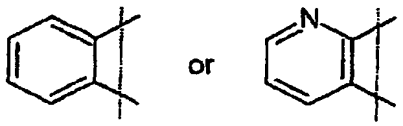
37. A novel compound of Formula I:



Formula I

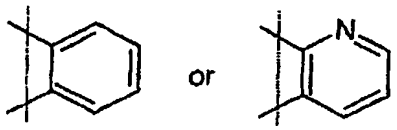
wherein,

"A" represents



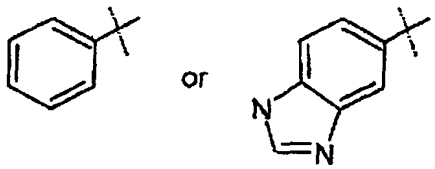
;

"B" represents



;

and "C" represents

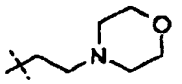
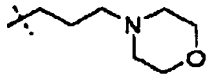


;

X and Y together represent $-CH_2-CH_2-$, $-CH_2-O-$, or $-O-CH_2-$;

"_____" represents a double bond;

R^1 represents halo, amino, oxo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxymethyl, difluromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, $SO_2NR^9R^{10}$ wherein R^9 represents (C_1-C_6)alkyl, (C_1-C_4)alkyl-(C_1-C_6)alkoxy , halo(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, aryl, (C_1-C_4)alkyl-aryl, heterocycle and R^{10} represents hydrogen or methyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a substituted or unsubstituted heterocycle; NH SO_2R^{11} wherein R^{11} represents amino, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy , (C_3-C_7)cycloalkyl, aryl, substituted aryl, heterocycle, or substituted heterocycle; $NHCOR^{12}$ wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy(C_1-C_6)alkyl, (C_1-C)alkyl-(C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, NH-methylamine, NH-dimethylamine, NH-ethylamine, or heterocycle; COR^{12} wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or hydroxy(C_1-C_6)alkyl; OR^{14} wherein R^{14} represents (C_1-C)alkyl-heterocycle; or a (C_1-C_4)alkyl-heterocycle represented by the formula:

 or 

provided that where "C" represents an aryl group then R^1 is other than oxo.;

further provided that where "C" represents a benzo-fused heterocycle then R^1 may also represent hydrogen;

R^2 represents hydrogen, halo, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, or (C_1-C_4)alkyl-heterocycle;

R^3 represents hydrogen, halo, or (C_1-C_6)alkyl;

R^4-R^7 each independently represent hydrogen, hydroxy, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or OR^{14} wherein R^{14} represents (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, (C_1-C_4)alkyl-heterocycle, or (C_1-C_4)alkyl-(C_3-C_7)cycloalkyl ;

R^8 represents hydrogen, halo, (C_1-C_6)alkyl, hydroxymethyl, (C_1-C_4)alkyl -(C_1-C_6)alkoxy , or COR^{12} wherein R^{12} represents (C_1-C_6)alkoxy; (C_3-C_7)cycloalkyl, phenyl, or substituted aryl;

further provided that where C represents a phenyl ring and R^1 represents halo then at least one of R^2 and R^3 is other than hydrogen, (C_1-C_6)alkyl, aryl, substituted aryl, (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, CHF_2, or CF_3; and

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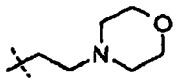
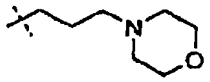
further provided that where C represents a six-membered ring and R^1 represents amino or $NHCOCH_3$ and R^2 and R^3 are each hydrogen, then R^1 is not bound at the 4-position of said six-membered ring,

or a pharmaceutically acceptable salt thereof.

38. The compound according to Claim 37 wherein "C" represents a phenyl ring and R^1 represents $SO_2NR^9R^{10}$ wherein R^9 represents (C_1-C_6)alkyl, (C_1-C_4)alkyl-(C_1-C_6)alkoxy , halo(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, aryl, (C_1-C_4)alkyl-aryl, heterocycle and R^{10} represents hydrogen or methyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a substituted or unsubstituted heterocycle; NH SO_2R^{11} wherein R^{11} represents amino, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy , (C_3-C_7)cycloalkyl, aryl, substituted aryl, heterocycle, or substituted heterocycle; $NHCOR^{12}$ wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy(C_1-C_6)alkyl, (C_1-C)alkyl-(C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, NH-methylamine, NH-dimethylamine, NH-ethylamine, or heterocycle; COR^{12} wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or hydroxy(C_1-C_6)alkyl; OR^{14} wherein R^{14} represents (C_1-C)alkyl-heterocycle; or a (C_1-C_4)alkyl-heterocycle represented by the formula:

 or  .

or a pharmaceutically acceptable salt thereof.

39. A compound according to any one of Claims 37 and 38 wherein when R^1 represents NH SO_2R^{11}, R^{11} represents methyl, ethyl, propyl, isopropyl, butyl, or 2-methyl propyl.

40. The compound according to Claim 39 wherein R^{11} represents methyl.

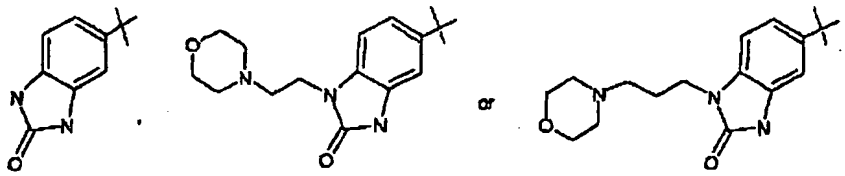
41. A compound according to any one of Claims 37 – 40 wherein R^2 represents hydrogen or (C_1-C_4)alkyl-heterocycle.

42. The compound according to Claim 41 wherein R^2 represents hydrogen.

43. A compound according to any one of Claims 37 – 42 wherein R^3 represents hydrogen.

44. A compound according to any one of claims 37, 41-43 wherein "C" represents a benzofused heterocycle having a non-hydrogen substituent at at least one of

R1-R3, wherein said benzofused heterocycle having a non-hydrogen substituent is given by the following:



45. A compound according to any one of Claims 37-44 wherein R^4 and R^6 each independently represent hydrogen, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or OR^{14} wherein R^{14} represents (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, (C_1-C_4)alkyl-heterocycle, or (C_1-C_4)alkyl-(C_3-C_7)cycloalkyl.

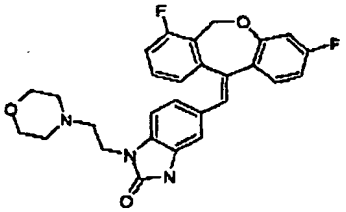
46. A compound according to any one of Claim 37- 45 wherein R^5 and R^7 each independently represent hydrogen, hydroxy, halo, (C_1-C_6)alkyl, or (C_1-C_6)alkoxy.

47. A compound according to any one of Claims 37-46 wherein R^8 represents hydrogen, halo, (C_1-C_6)alkyl, (C_1-C_4)alkyl -(C_1-C_6)alkoxy , or (C_3-C_7)cycloalkyl.

48. The compound according to Claim 47 wherein R^8 represents halo (C_1-C_6)alkyl, (C_1-C_4)alkyl -(C_1-C_6)alkoxy.

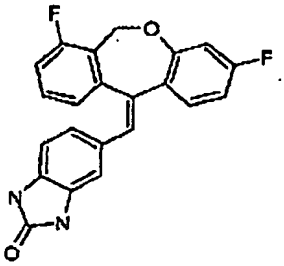
49. The compound according to Claim 47 wherein R^8 represents hydrogen.

50. A compound of the formula



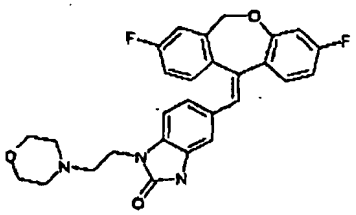
or a pharmaceutically acceptable salt thereof.

51. A compound of the formula



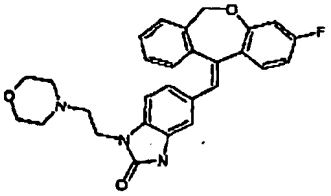
or a pharmaceutically acceptable salt thereof.

52. A compound of the formula



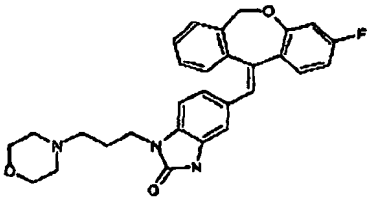
or a pharmaceutically acceptable salt thereof.

53. A compound of the formula



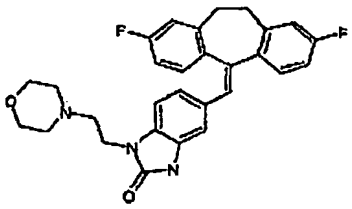
or a pharmaceutically acceptable salt thereof.

54. A compound of the formula



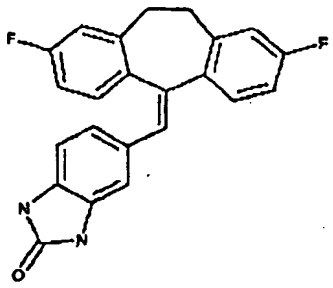
or a pharmaceutically acceptable salt thereof.

55. A compound of the formula



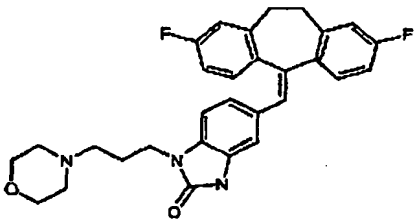
or a pharmaceutically acceptable salt thereof.

56. A compound of the formula



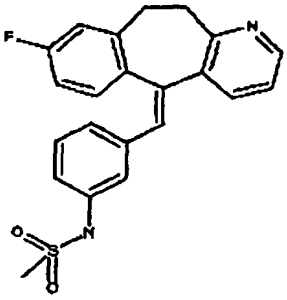
or a pharmaceutically acceptable salt thereof.

57. A compound of the formula



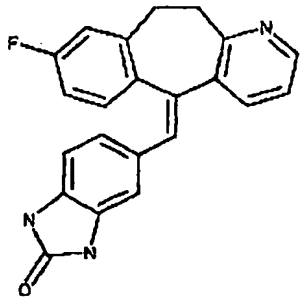
or a pharmaceutically acceptable salt thereof.

58. A compound of the formula



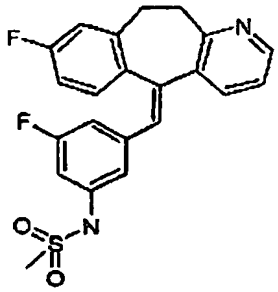
or a pharmaceutically acceptable salt thereof.

59. A compound of the formula



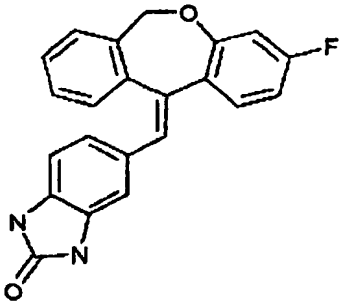
or a pharmaceutically acceptable salt thereof.

60. A compound of the formula



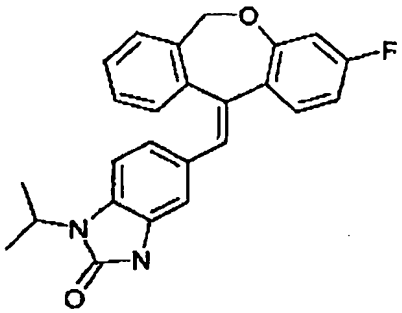
or a pharmaceutically acceptable salt thereof.

61. A compound of the formula



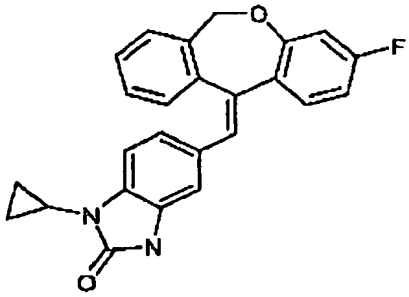
or a pharmaceutically acceptable salt thereof.

62. A compound of the formula



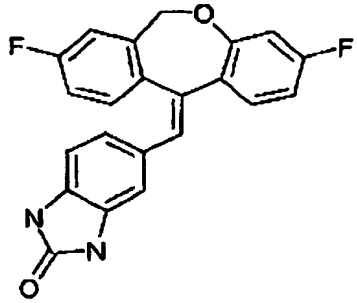
or a pharmaceutically acceptable salt thereof.

63. A compound of the formula



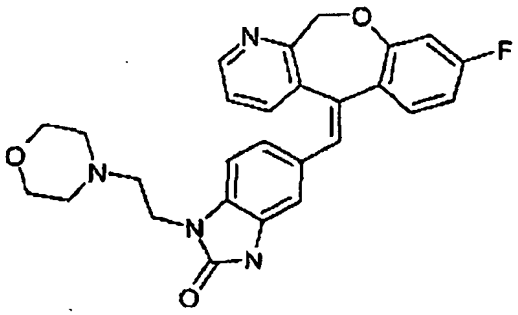
or a pharmaceutically acceptable salt thereof.

64. A compound of the formula



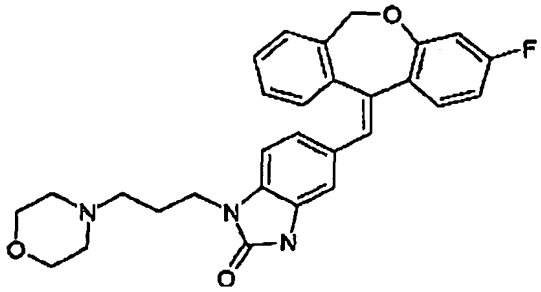
or a pharmaceutically acceptable salt thereof.

65. A compound of the formula



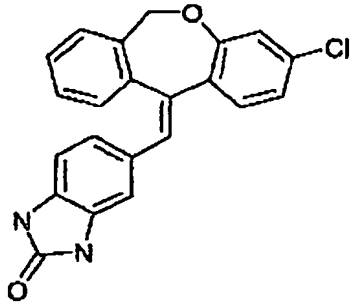
or a pharmaceutically acceptable salt thereof.

66. A compound of the formula



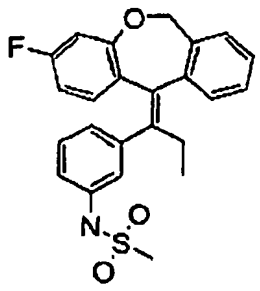
or a pharmaceutically acceptable salt thereof.

67. A compound of the formula



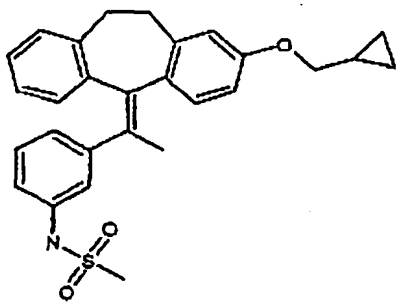
or a pharmaceutically acceptable salt thereof.

68. A compound of the formula



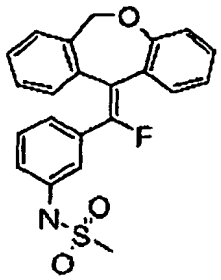
or a pharmaceutically acceptable salt thereof.

69. A compound of the formula



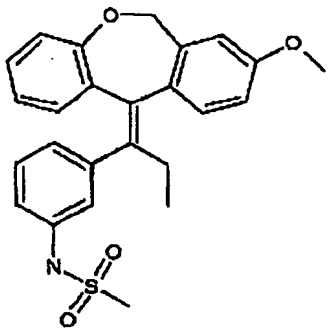
or a pharmaceutically acceptable salt thereof.

70. A compound of the formula



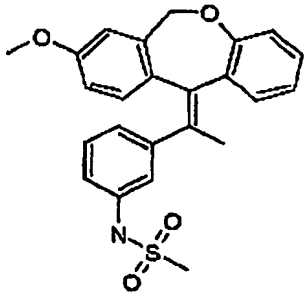
or a pharmaceutically acceptable salt thereof.

71. A compound of the formula



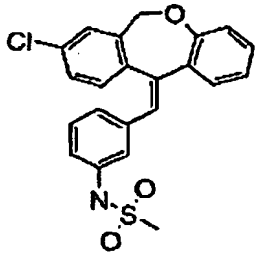
or a pharmaceutically acceptable salt thereof.

72. A compound of the formula



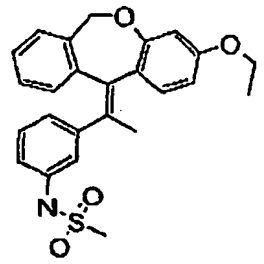
or a pharmaceutically acceptable salt thereof.

73. A compound of the formula



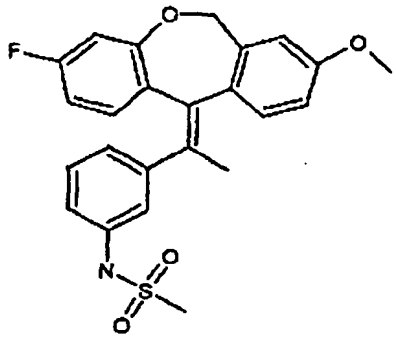
or a pharmaceutically acceptable salt thereof.

74. A compound of the formula



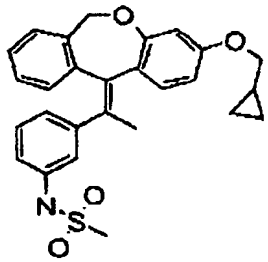
or a pharmaceutically acceptable salt thereof.

75. A compound of the formula



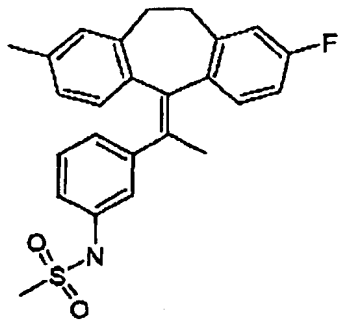
or a pharmaceutically acceptable salt thereof.

76. A compound of the formula



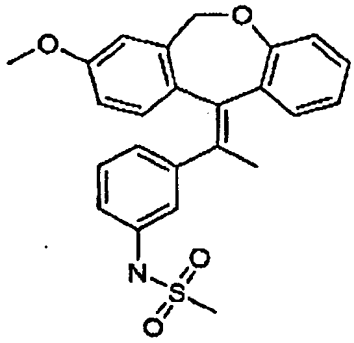
or a pharmaceutically acceptable salt thereof.

77. A compound of the formula



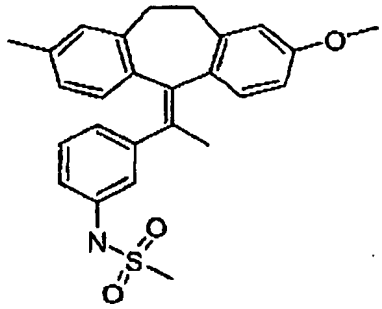
or a pharmaceutically acceptable salt thereof.

78. A compound of the formula



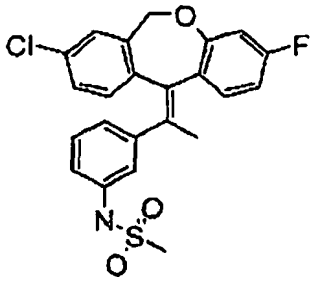
or a pharmaceutically acceptable salt thereof.

79. A compound of the formula



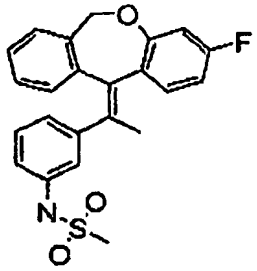
or a pharmaceutically acccptable salt thereof.

80. A compound of the formula



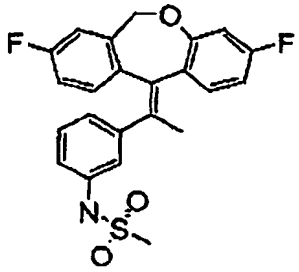
or a pharmaceutically acceptable salt thereof.

81. A compound of the formula



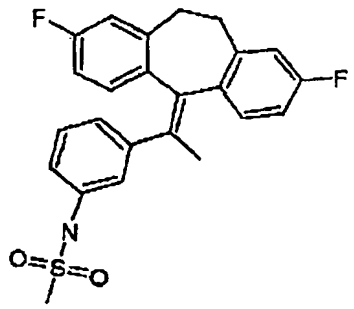
or a pharmaceutically acceptable salt thereof.

82. A compound of the formula



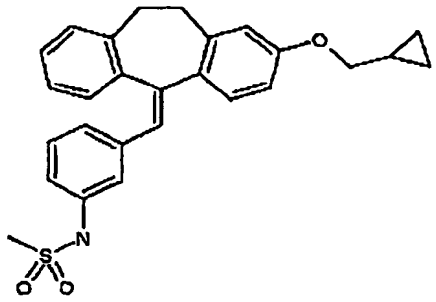
or a pharmaceutically acceptable salt thereof.

83. A compound of the formula



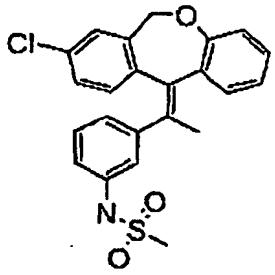
or a pharmaceutically acceptable salt thereof.

84. A compound of the formula



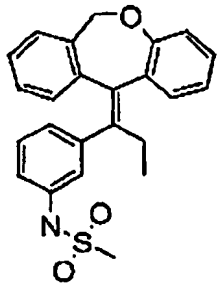
or a pharmaceutically acceptable salt thereof.

85. A compound of the formula



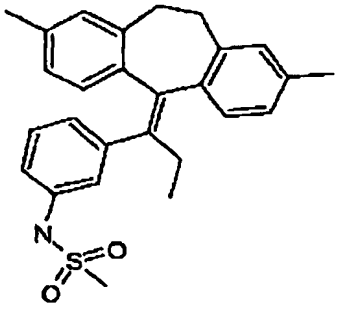
or a pharmaceutically acceptable salt thereof.

86. A compound of the formula



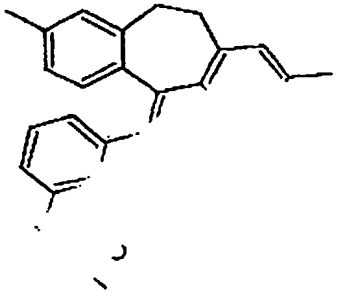
or a pharmaceutically acceptable salt thereof.

87. A compound of the formula



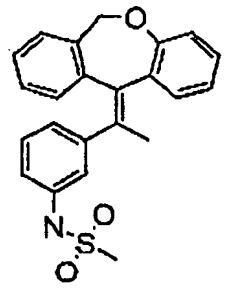
or a pharmaceutically acceptable salt thereof.

88. A compound of the formula



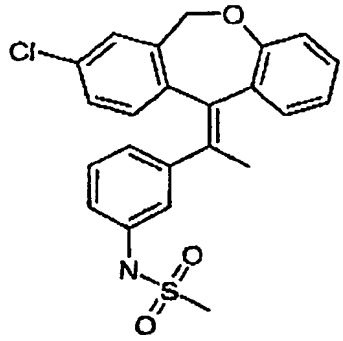
or a pharmaceutically acceptable salt thereof.

89. A compound of the formula



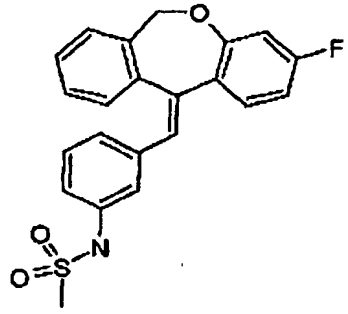
or a pharmaceutically acceptable salt thereof.

90. A compound of the formula



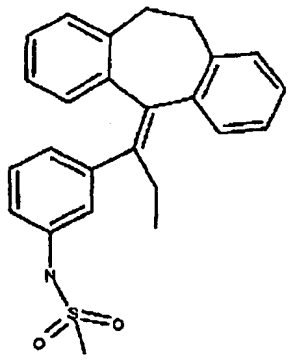
or a pharmaceutically acceptable salt thereof.

91. A compound of the formula



or a pharmaceutically acceptable salt thereof.

92. A compound of the formula



or a pharmaceutically acceptable salt thereof.

93. A method of treating a physiological disorder susceptible to mineralocorticoid or glucocorticoid receptor modulation wherein said disorder is selected from the group consisting of Conn's Syndrome, primary and secondary hyperaldosteronism, increased sodium retention, increased magnesium and potassium excretion (diuresis), increased water retention, hypertension (isolated systolic and combined systolic/diastolic), arrhythmias, myocardial fibrosis, myocardial infarction, Bartter's Syndrome, disorders associated with excess catecholamine levels, diastolic and systolic congestive heart failure (CHF), psychoses, cognitive disorders, memory disturbances, depression, bipolar disorder, anxiety disorders, personality disorders, breast cancer, peripheral vascular disease, diabetic nephropathy, cirrhosis with edema and ascites, esophageal varicies, Addison's Disease, muscle weakness, increased melanin pigmentation of the skin, weight loss, hypotension, hypoglycemia, Cushing's Syndrome, obesity, hypertension, glucose intolerance, hyperglycemia, diabetes mellitus, osteoporosis, polyuria, polydipsia, inflammation, autoimmune disorders, tissue rejection associated with organ transplant, malignancies such as leukemias and lymphomas, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, polyarteritis nodosa, granulomatous polyarteritis, inhibition of myeloid cell lines, immune proliferation/apoptosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hypergylcemia, acute adrenal insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency, congenital adrenal hyperplasia, cerebral edema, thrombocytopenia, and Little's syndrome, systemic inflammation, inflammatory bowel disease, systemic lupus erythematosus, discoid lupus erythematosus, polyartitis nodosa, Wegener's granulomatosis, giant cell arthritis, rheumatoid arthritis, osteoarthritis, hay fever, allergic rhinitis, contact dermatitis, atopic dermatitis, exfoliative

dermatitis, urticaria, angioneurotic edema, chronic obstructive pulmonary disease, asthma, tendonitis, bursitis, Crohn's disease, ulcerative colitis, autoimmune chronic active hepatitis, hepatitis, cirrhosis, inflammatory scalp alopecia, panniculitis, psoriasis, inflamed cysts, pyoderma gangrenosum, pemphigus vulgaris, bullous pemphigoid, dermatomyositis, eosinophilic fasciitis, relapsing polychondritis, inflammatory vasculitis, sarcoidosis, Sweet's disease, type 1 reactive leprosy, capillary hemangiomas, lichen planus, , erythema nodosum, acne, hirsutism, toxic epidermal necrolysis, erythema multiform, cutaneous T-cell lymphoma, emphysema, Alzheimer's Disease, and multiple sclerosis., comprising administering to a patient in need thereof an effective amount of a novel compound of Formula I according to claim 37.

94. The method according to claim 93, wherein said disorder is diastolic or systolic congestive heart failure, inflammation, rheumatoid arthritis, an autoimmune disorder, asthma, or chronic obstructive pulmonary disease

95. The method according to claim 94, wherein said disorder is diastolic or systolic congestive heart failure or rheumatoid arthritis.

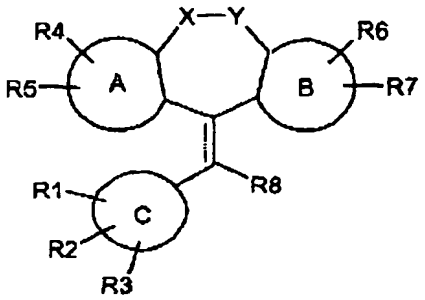
96. A method of modulating a steroid hormone nuclear receptor , wherein said steroid nuclear receptor is the mineralocorticoid receptor or the glucocorticoid receptor , comprising administering to a patient in need thereof an effective amount of a compound of Formula I according to Claim 37.

97. A pharmaceutical composition comprising an effective amount of a compound of Formula I according to Claim 37 in combination with a pharmaceutically acceptable carrier.

98. The use of a compound of Formula I according to Claim 37 for the manufacture of a medicament for the treatment of diastolic or systolic congestive heart failure or rheumatoid arthritis.

ABSTRACT

The present invention relates to methods of treating pathological disorders susceptible to steroid hormone nuclear receptor modulation comprising administering to a patient in need thereof an effective amount of a compound of the formula:



Formula I

or a pharmaceutically acceptable salt thereof. In addition, the present invention provides novel pharmaceutical compounds of Formula I, including the pharmaceutically acceptable salts thereof, as well as pharmaceutical compositions which comprise as an active ingredient a compound of Formula I.